<u>Parallel Session</u>
Physiology I

PARTICLE-BASED MODEL OF MICROVASCULAR THROMBUS FORMATION DEMONSTRATES THE ROLE OF THE INTERPLAY BETWEEN PLATELET ADHESIVE RECEPTORS

Valeriia Kaneva

lerakaneva@gmail.com

Faculty of Physics, Lomonosov Moscow State University, Moscow, Russian Federation

Joint work with Dmitry Yu. Nechipurenko (Faculty of Physics, Lomonosov Moscow State University, Moscow, Russian Federation), Peter V. Trifanov (Faculty of Physics, Lomonosov Moscow State University, Moscow, Russian Federation), Fazoil I. Ataullakhanov (Center for Theoretical Problems of Physicochemical Pharmacology, Moscow, Russian Federation), Joanne L. Dunster (Department of Mathematics and Statistics, University of Reading, Reading, Berkshire, United Kingdom), Jonathan M. Gibbins (Institute for Cardiovascular and Metabolic Research and School of Biological Sciences, University of Reading, Reading, Berkshire, United Kingdom), Mikhail A. Panteleev (Center for Theoretical Problems of Physicochemical Pharmacology, Moscow, Russian Federation)

Keywords: Particle-based model, Stochastic modelling, Thrombus, Platelets, Biorheology.

Platelets are anucleated cellular fragments produced in bone marrow. Upon vessel wall damage, they adhere to the injury site, forming a thrombus - a plug that acts as a physical obstacle for blood loss. However, in some conditions thrombus can occlude a vessel, what might lead to a number of pathological consequences. Understanding of the mechanisms that regulate thrombus size can significantly improve our approaches for curing a whole variety of diseases, including ischemic strokes and myocardial infarctions.

According to in-vivo experiments in mice, microvascular thrombus is heterogeneous: platelets of its inner firm part (called core) are closely packed, while loose outer part of thrombus (called shell) is unstable and possess a fluid-like behavior. The origin of platelet thrombus heterogeneity and dynamics of thrombus shell are still poorly understood. Despite the abundance of experimental data covering various features of platelet interaction through various receptors in different states, a link between this knowledge and experimental observations of thrombus behavior is still missing. The aim of our research was to investigate whether the nature of thrombus structure and dynamics can be explained by physical properties of platelet interactions through their adhesive receptors.

We created a 2d model of thrombus formation in which platelets were represented by discoid particles 2 μm in diameter. Blood was considered as incompressible Newtonian fluid. The model takes into account two types of inter-platelet interaction: primary reversible (glycoprotein-Ib-mediated) and secondary, which intensify with the increase of platelet activation (integrins-mediated). The first type of interaction is described by stochastically

associating and dissociating springs, while the second type is represented by deterministic Morse potential, which is often used to describe interaction between cells. Platelet activation was described as a time-dependent process. Parameters of platelet interaction models were acquired based on experimental data. We inferred stochastic springs model parameters using experiments on platelet rolling over adhesive surface. It is important to note that a simpler deterministic model failed to describe such experiments. Parameters of Morse potential were derived fitting experimental data on forces between single activated platelets. Computational modeling of thrombus formation produced the following results:

1. Thrombus is heterogeneous, having stable inner and fluid-like outer part. New platelets do not adhere instantly, but roll over the thrombus surface, thereby forming specific thrombus shape.

2. Model with only partial platelet activation demonstrates cycles of growths followed by disruptions of thrombus, consistent with the experimental findings.

3. Stochastic interaction is likely responsible for fluid-like mobility of thrombus exterior. Thus, we designed the first model describing fluid-like behavior of thrombus shell. Our model shows the necessity and sufficiency of the two different types of interactions for the description of the important features of thrombus structure and dynamics. Our study also emphasizes the importance of stochastic description of cell-cell interaction.

TUNING CRITICAL EXCITATIONS IN STIFF CARDIAC MODELS

CHRISTOPHER D. MARCOTTE

c.marcotte@exeter.ac.uk

Living Systems Institute, University of Exeter, Stocker Road, Exeter, EX4 4QD, UK

Joint work with Vadim Biktashev and Peter Ashwin (University of Exeter).

Keywords: Cardiac dynamics, Excitable media, Critical excitation.

Excitable models of cardiac tissue typically couple dynamical features on wildly disparate spatial and temporal scales, leading to patterns which resist classical methods of analysis. Semi-analytical techniques [1] may address this difficulty and characterize excitability properties of cardiac models, for which stiff models present a numerical challenge. An essential ingredient of these techniques is the stability spectrum of the simplest coherent structures produced by these models. I will discuss techniques for computing these solutions in several stiff models of cardiac tissue dynamics and use their stability characteristics to predict excitability properties of the model. Additionally, I explore how these techniques are applied to models with non-Tikhonov features and the application of these techniques to understanding conduction block.

References

[1] Bezekci B, Idris I, Simitev RD, Biktashev VN. (2015). *Semi-analytical approach to criteria for ignition of excitation waves*, Physical Review E 92, 042917.

COMPUTER SIMULATIONS OF CELL ADHESION TO SURFACES WITH MICRORELIEF

ALEKSEY V. BELYAEV

aleksey_belyaev@yahoo.com

Faculty of Physics, M.V. Lomonosov Moscow State University,
1, Leninskiye Gory, 119991 Moscow, Russia

Keywords: Adhesion, Computer modelling, Cell biomechanics, Microrelief.

The adhesion of living cells is ubiquitous, but it is not always favourable. For instance, surfaces of medical devices can be colonized by bacteria and cause infection, or blood-processing biomicrofluidic devices can be blocked by the thrombus as a result of blood platelet adhesion. On the other hand, in some cases the strong attachment of cells is needed, e.g. growing tissues on artificial scaffolds. One of the novel strategies to control cell adhesion is the modification of surface relief of the material. In the present work the ligand-receptor adhesion of a spherical deformable cell to a micro-rough surface immersed in viscous fluid was studied by means of computer modelling. The Lattice Boltzmann [1] method was used to model the fluid flows around the cell and Lagrangian Particle Dynamics [2] was used to track cell membrane position and shape in time. The adhesive bonds between cell membrane receptors and the substrate were implemented according to stochastic springs model, following [3]. Three regimes of adhesion were observed. Generally, in the presented model superhydrophilic rough surfaces tend to be more sticky as compared to flat walls. The obtained numerical results provide the theoretical basis for the design of artificial antibacterial and hemocompatible surfaces.

References

[1] S. Succi. *The Lattice Boltzmann Equation for Fluid Dynamics and Beyond.* Oxford University Press, New-York, 2001.

[2] I. Cimrak, M. Gusenbauer and T. Schrefl. (2012). *Modelling and simulation of processes in microfluidic devices for biomedical applications*, Computers and Mathematics with Applications 64, 278–288.

[3] D.A. Hammer and S.M. Apte. (1992). *Simulation of cell rolling and adhesion on surfaces in shear flow: general results and analysis of selectin-mediated neutrophil adhesion*, Biophys. J. 63, 35–57.

APPEARANCE OF A CHIRAL STRUCTURE IN CARDIAC LOOPING OF THE EMBRYONIC HEART

Hisao Honda

hihonda@hyogo-dai.ac.jp

Kobe University Graduate School of Midicine, Japan and RIKEN CDB, Japan

Joint work with Takaya Abe (RIKEN CLST) and Toshihiko Fujimori (NIBB, RIKEN CLST).

Keywords: Cardiac loop, Mechano-physical cell model, Left-handed helix.

We are studying a mechanism of cardiac looping of the embryonic heart using a mechano-physical cell model, the cell-based vertex dynamics for tissues. There was a simple straight tube as an initial condition of computer simulation. Polygons (cells) were packed on the tube surface without gaps or overlaps and morphogenesis of polygonal patterns was described by the vertex dynamics. We assumed two factors that may cause a straight tube forming a helical loop. (1) Ventral bending of the tube by cell division. Cells on the ventral half of the tube were assumed to divide longitudinally. Then the ventral side of the tube elongated and the tube bent. (2) Cells in the posterior region of the tube were assumed to migrate leftward. Computer simulations based on the two assumptions showed that the straight tube looped to be a left-handed helix. The result is worth notice, because although the two factors respectively do not involve chiral properties, combination of the two factors produces chirality of left-handed helix looping. Experimental evidences of the two factors were discussed.